## SEQUENCE LISTING

- <110> SUZUKI, Toshiharu et al.
- <120> MARKER PEPTIDE FOR ALZHEIMER'S DISEASE
- <130> 3749-0112PUS1
- <140> US 10/577,008
- <141> 2006-04-25
- <150> PCT/JP2004/016209
- <151> 2004-11-01
- <150> JP 2003/375363
- <151> 2003-11-05
- <160> 17
- <170> PatentIn version 3.5
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Asn Asp Asn Thr Val Leu Leu Asp Pro Pro Leu Ile Ala Leu Asp Lys 50 55 60

Asp Ala Pro Leu Arg Phe Ala Gly Glu Ile Cys Gly Phe Lys Ile His 65 70 75 80

Gly Gln Asn Val Pro Phe Asp Ala Val Val Val Asp Lys Ser Thr Gly 85 90 95

Glu Gly Val Ile Arg Ser Lys Glu Lys Leu Asp Cys Glu Leu Gln Lys 100 105 110

Asp Tyr Ser Phe Thr Ile Gln Ala Tyr Asp Cys Gly Lys Gly Pro Asp

Gly Thr Asn Val Lys Lys Ser His Lys Ala Thr Val His Ile Gln Val Asn Asp Val Asn Glu Tyr Ala Pro Val Phe Lys Glu Lys Ser Tyr Lys Ala Thr Val Ile Glu Gly Lys Gln Tyr Asp Ser Ile Leu Arg Val Glu Ala Val Asp Ala Asp Cys Ser Pro Gln Phe Ser Gln Ile Cys Ser Tyr Glu Ile Ile Thr Pro Asp Val Pro Phe Thr Val Asp Lys Asp Gly Tyr Ile Lys Asn Thr Glu Lys Leu Asn Tyr Gly Lys Glu His Gln Tyr Lys Leu Thr Val Thr Ala Tyr Asp Cys Gly Lys Lys Arg Ala Thr Glu Asp Val Leu Val Lys Ile Ser Ile Lys Pro Thr Cys Thr Pro Gly Trp Gln Gly Trp Asn Asn Arg Ile Glu Tyr Glu Pro Gly Thr Gly Ala Leu Ala Val Phe Pro Asn Ile His Leu Glu Thr Cys Asp Glu Pro Val Ala Ser Val Gln Ala Thr Val Glu Leu Glu Thr Ser His Ile Gly Lys Gly Cys Asp Arg Asp Thr Tyr Ser Glu Lys Ser Leu His Arg Leu Cys Gly Ala Ala Ala Gly Thr Ala Glu Leu Leu Pro Ser Pro Ser Gly Ser Leu Asn 

Trp Thr Met Gly Leu Pro Thr Asp Asn Gly His Asp Ser Asp Gln Val

Phe	Glu	Phe 355	Asn	Gly	Thr	Gln	Ala 360	Val	Arg	Ile	Pro	Asp 365	Gly	Val	Val
Ser	Val 370	Ser	Pro	Lys	Glu	Pro 375	Phe	Thr	Ile	Ser	Val 380	Trp	Met	Arg	His
Gly 385	Pro	Phe	Gly	Arg	Lys 390	Lys	Glu	Thr	Ile	Leu 395	Cys	Ser	Ser	Asp	Lys 400
Thr	Asp	Met	Asn	Arg 405	His	His	Tyr	Ser	Leu 410	Tyr	Val	His	Gly	Cys 415	Arg
Leu	Ile	Phe	Leu 420	Phe	Arg	Gln	Asp	Pro 425	Ser	Glu	Glu	Lys	Lys 430	Tyr	Arg
Pro	Ala	Glu 435	Phe	His	Trp	Lys	Leu 440	Asn	Gln	Val	Cys	Asp 445	Glu	Glu	Trp
His	His 450	Tyr	Val	Leu	Asn	Val 455	Glu	Phe	Pro	Ser	Val 460	Thr	Leu	Tyr	Val
Asp 465	Gly	Thr	Ser	His	Glu 470	Pro	Phe	Ser	Val	Thr 475	Glu	Asp	Tyr	Pro	Leu 480
His	Pro	Ser	Lys	Ile 485	Glu	Thr	Gln	Leu	Val 490	Val	Gly	Ala	Cys	Trp 495	Gln
Glu	Phe	Ser	Gly 500	Val	Glu	Asn	Asp	Asn 505	Glu	Thr	Glu	Pro	Val 510	Thr	Val
Ala	Ser	Ala 515	Gly	Gly	Asp	Leu	His 520	Met	Thr	Gln	Phe	Phe 525	Arg	Gly	Asn
Leu	Ala 530	Gly	Leu	Thr	Leu	Arg 535	Ser	Gly	Lys	Leu	Ala 540	Asp	Lys	Lys	Val
Ile 545	Asp	Cys	Leu	Tyr	Thr 550	Cys	Lys	Glu	Gly	Leu 555	Asp	Leu	Gln	Val	Leu 560
Glu	Asp	Ser	Gly	Arg 565	Gly	Val	Gln	Ile	Gln 570	Ala	His	Pro	Ser	Gln 575	Leu

Val Leu Thr Leu Glu Gly Glu Asp Leu Gly Glu Leu Asp Lys Ala Met Gln His Ile Ser Tyr Leu Asn Ser Arg Gln Phe Pro Thr Pro Gly Ile Arg Arg Leu Lys Ile Thr Ser Thr Ile Lys Cys Phe Asn Glu Ala Thr Cys Ile Ser Val Pro Pro Val Asp Gly Tyr Val Met Val Leu Gln Pro Glu Glu Pro Lys Ile Ser Leu Ser Gly Val His His Phe Ala Arg Ala Ala Ser Glu Phe Glu Ser Ser Glu Gly Val Phe Leu Phe Pro Glu Leu Arg Ile Ile Ser Thr Ile Thr Arg Glu Val Glu Pro Glu Gly Asp Gly Ala Glu Asp Pro Thr Val Gln Glu Ser Leu Val Ser Glu Glu Ile Val His Asp Leu Asp Thr Cys Glu Val Thr Val Glu Glu Glu Leu Asn His Glu Gln Glu Ser Leu Glu Val Asp Met Ala Arg Leu Gln Gln Lys Gly Ile Glu Val Ser Ser Glu Leu Gly Met Thr Phe Thr Gly Val Asp Thr Met Ala Ser Tyr Glu Glu Val Leu His Leu Leu Arg Tyr Arg Asn Trp His Ala Arg Ser Leu Leu Asp Arg Lys Phe Lys Leu Ile Cys Ser Glu Leu Asn Gly Arg Tyr Ile Ser Asn Glu Phe Lys Val Glu Val 

Asn Val Ile His Thr Ala Asn Pro Met Glu His Ala Asn His Met Ala 810 Ala Gln Pro Gln Phe Val His Pro Glu His Arg Ser Phe Val Asp Leu 825 Ser Gly His Asn Leu Ala Asn Pro His Pro Phe Ala Val Val Pro Ser 835 Thr Ala Thr Val Val Ile Val Val Cys Val Ser Phe Leu Val Phe Met 850 855 860 Ile Ile Leu Gly Val Phe Arg Ile Arg Ala Ala His Arg Arg Thr Met 865 870 Arg Asp Gln Asp Thr Gly Lys Glu Asn Glu Met Asp Trp Asp Asp Ser 890 895 Ala Leu Thr Ile Thr Val Asn Pro Met Glu Thr Tyr Glu Asp Gln His 900 905 915 Gly Glu Glu Glu Asp Asp Ile Thr Ser Ala Glu Ser Glu Ser Ser Glu 930 935 Glu Glu Glu Gly Glu Gln Gly Asp Pro Gln Asn Ala Thr Arg Gln Gln 945 950 Gln Leu Glu Trp Asp Asp Ser Thr Leu Ser Tyr 965 <210> 2 <211> 968 <212> PRT <213> human <400> 2 Met Val Leu Gly Cys Glu Leu Ser Gly Ser Thr Arg Val Val Val Gly Val Glu Ala Leu Leu Thr Gly Ala Ser Ser Pro Leu Pro Gly Val Gly

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Ser Trp Gln Gly Trp Asn Lys Arg Ile Glu Tyr Ala Pro Gly Ala Gly Ser Leu Ala Leu Phe Pro Gly Ile Arg Leu Glu Thr Cys Asp Glu Pro Leu Trp Asn Ile Gln Ala Thr Ile Glu Leu Gln Thr Ser His Val Ala Lys Gly Cys Asp Arg Asp Asn Tyr Ser Glu Arg Ala Leu Arg Lys Leu Cys Gly Ala Ala Thr Gly Glu Val Asp Leu Leu Pro Met Pro Gly Pro Asn Ala Asn Trp Thr Ala Gly Leu Ser Val His Tyr Ser Gln Asp Ser Ser Leu Ile Tyr Trp Phe Asn Gly Thr Gln Ala Val Gln Val Pro Leu Gly Gly Pro Ser Gly Leu Gly Ser Gly Pro Gln Asp Ser Leu Ser Asp His Phe Thr Leu Ser Phe Trp Met Lys His Gly Val Thr Pro Asn Lys Gly Lys Lys Glu Glu Glu Thr Ile Val Cys Asn Thr Val Gln Asn Glu Asp Gly Phe Ser His Tyr Ser Leu Thr Val His Gly Cys Arg Ile Ala Phe Leu Tyr Trp Pro Leu Leu Glu Ser Ala Arg Pro Val Lys Phe Leu Trp Lys Leu Glu Gln Val Cys Asp Asp Glu Trp His His Tyr Ala Leu Asn Leu Glu Phe Pro Thr Val Thr Leu Tyr Thr Asp Gly Ile Ser Phe 

Asp	Pro	Ala	Leu	Ile 485	His	Asp	Asn	Gly	Leu 490	Ile	His	Pro	Pro	Arg 495	Arg
Glu	Pro	Ala	Leu 500	Met	Ile	Gly	Ala	Cys 505	Trp	Thr	Glu	Glu	Lys 510	Asn	Lys
Glu	Lys	Glu 515	Lys	Gly	Asp	Asn	Ser 520	Thr	Asp	Thr	Thr	Gln 525	Gly	Asp	Pro
Leu	Ser 530	Ile	His	His	Tyr	Phe 535	His	Gly	Tyr	Leu	Ala 540	Gly	Phe	Ser	Val
Arg 545	Ser	Gly	Arg	Leu	Glu 550	Ser	Arg	Glu	Val	Ile 555	Glu	Cys	Leu	Tyr	Ala 560
Cys	Arg	Glu	Gly	Leu 565	Asp	Tyr	Arg	Asp	Phe 570	Glu	Ser	Leu	Gly	Lys 575	Gly
Met	Lys	Val	His 580	Val	Asn	Pro	Ser	Gln 585	Ser	Leu	Leu	Thr	Leu 590	Glu	Gly
Asp	Asp	Val 595	Glu	Thr	Phe	Asn	His 600	Ala	Leu	Gln	His	Val 605	Ala	Tyr	Met
Asn	Thr 610	Leu	Arg	Phe	Ala	Thr 615	Pro	Gly	Val	Arg	Pro 620	Leu	Arg	Leu	Thr
Thr 625	Ala	Val	Lys	Cys	Phe 630	Ser	Glu	Glu	Ser	Cys 635	Val	Ser	Ile	Pro	Glu 640
Val	Glu	Gly	Tyr	Val 645	Val	Val	Leu	Gln	Pro 650	Asp	Ala	Pro	Gln	Ile 655	Leu
Leu	Ser	Gly	Thr 660	Ala	His	Phe	Ala	Arg 665	Pro	Ala	Val	Asp	Phe 670	Glu	Gly
Thr	Asn	Gly 675	Val	Pro	Leu	Phe	Pro 680	Asp	Leu	Gln	Ile	Thr 685	Cys	Ser	Ile
Ser	His 690	Gln	Val	Glu	Ala	Lys 695	Lys	Asp	Glu	Ser	Trp 700	Gln	Gly	Thr	Val
Thr	Asp	Thr	Arg	Met	Ser	Asp	Glu	Ile	Val	His	Asn	Leu	Asp	Gly	Cys

705	710	715	720
703	710	110	120

Glu	Ile	Ser	Leu	Val	Gly	Asp	Asp	Leu	Asp	Pro	Glu	Arg	Glu	Ser	Leu
				725					730					735	

- Leu Leu Asp Thr Thr Ser Leu Gln Gln Arg Gly Leu Glu Leu Thr Asn 740 745 750
- Thr Ser Ala Tyr Leu Thr Ile Ala Gly Val Glu Ser Ile Thr Val Tyr 755 760 765
- Glu Glu Ile Leu Arg Gln Ala Arg Tyr Arg Leu Arg His Gly Ala Ala 770 780
- Leu Tyr Thr Arg Lys Phe Arg Leu Ser Cys Ser Glu Met Asn Gly Arg 785 790 795 800
- Tyr Ser Ser Asn Glu Phe Ile Val Glu Val Asn Val Leu His Ser Met 805 810 815
- Asn Arg Val Ala His Pro Ser His Val Leu Ser Ser Gln Gln Phe Leu 820 825 830
- His Arg Gly His Gln Pro Pro Pro Glu Met Ala Gly His Ser Leu Ala 835 840 845
- Ser Ser His Arg Asn Ser Met Ile Pro Ser Ala Ala Thr Leu Ile Ile 850 855 860
- Val Val Cys Val Gly Phe Leu Val Leu Met Val Val Leu Gly Leu Val 865 870 875 880
- Arg Ile His Ser Leu His Arg Arg Val Ser Gly Ala Gly Gly Pro Pro  $885 \\ 890 \\ 895$
- Gly Ala Ser Ser Asp Pro Lys Asp Pro Asp Leu Phe Trp Asp Asp Ser 900 905 910
- Ala Leu Thr Ile Ile Val Asn Pro Met Glu Ser Tyr Gln Asn Arg Gln 915 920 925
- Ser Cys Val Thr Gly Ala Val Gly Gly Gln Gln Glu Asp Glu Asp Ser 930 935 940

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Val Val His Ile Gln Val Lys Asp Val Asn Glu Phe Ala Pro Thr Phe

150

145

Ser Asp Ser Glu Val Ala Asp Ser Pro Ser Ser Asp Glu Arg Arg Ile

Lys Glu Pro Ala Tyr Lys Ala Val Val Thr Glu Gly Lys Ile Tyr Asp Ser Ile Leu Gln Val Glu Ala Ile Asp Glu Asp Cys Ser Pro Gln Tyr Ser Gln Ile Cys Asn Tyr Glu Ile Val Thr Thr Asp Val Pro Phe Ala Ile Asp Arg Asn Gly Asn Ile Arg Asn Thr Glu Lys Leu Ser Tyr Asp Lys Gln His Gln Tyr Glu Ile Leu Val Thr Ala Tyr Asp Cys Gly Gln Lys Pro Ala Ala Gln Asp Thr Leu Val Gln Val Asp Val Lys Pro Val Cys Lys Pro Gly Trp Gln Asp Trp Thr Lys Arg Ile Glu Tyr Gln Pro Gly Ser Gly Ser Met Pro Leu Phe Pro Ser Ile His Leu Glu Thr Cys Asp Gly Ala Val Ser Ser Leu Gln Ile Val Thr Glu Leu Gln Thr Asn Tyr Ile Gly Lys Gly Cys Asp Arg Glu Thr Tyr Ser Glu Lys Ser Leu Gln Lys Leu Cys Gly Ala Ser Ser Gly Ile Ile Asp Leu Leu Pro Ser Pro Ser Ala Ala Thr Asn Trp Thr Ala Gly Leu Leu Val Asp Ser Ser Glu Met Ile Phe Lys Phe Asp Gly Arg Gln Gly Ala Lys Ile Pro Asp Gly Ile Val Pro Lys Asn Leu Thr Asp Gln Phe Thr Ile Thr Met Trp Met Lys His Gly Pro Ser Pro Gly Val Arg Ala Glu Lys Glu Thr Ile

385	390	395	400

Leu	Cys	Asn	Ser	Asp	Lys	Thr	Glu	Met	Asn	Arg	His	His	Tyr	Ala	Leu
				405					410					415	

- Tyr Val His Asn Cys Arg Leu Val Phe Leu Leu Arg Lys Asp Phe Asp 420 425 430
- Gln Ala Asp Thr Phe Arg Pro Ala Glu Phe His Trp Lys Leu Asp Gln 435 440 445
- Ile Cys Asp Lys Glu Trp His Tyr Tyr Val Ile Asn Val Glu Phe Pro 450 455 460
- Val Val Thr Leu Tyr Met Asp Gly Ala Thr Tyr Glu Pro Tyr Leu Val 465 470 475 480
- Thr Asn Asp Trp Pro Ile His Pro Ser His Ile Ala Met Gln Leu Thr 485 490 495
- Val Gly Ala Cys Trp Gln Gly Gly Glu Val Thr Lys Pro Gln Phe Ala 500 505 510
- Gln Phe Phe His Gly Ser Leu Ala Ser Leu Thr Ile Arg Pro Gly Lys 515 520 525
- Met Glu Ser Gln Lys Val Ile Ser Cys Leu Gln Ala Cys Lys Glu Gly 530 535 540
- Leu Asp Ile Asn Ser Leu Glu Ser Leu Gly Gln Gly Ile Lys Tyr His 545 550 555 560
- Phe Asn Pro Ser Gln Ser Ile Leu Val Met Glu Gly Asp Asp Ile Gly 565 570 575
- Asn Ile Asn Arg Ala Leu Gln Lys Val Ser Tyr Ile Asn Ser Arg Gln 580 585 590
- Phe Pro Thr Ala Gly Val Arg Arg Leu Lys Val Ser Ser Lys Val Gln  $595 \hspace{1.5cm} 600 \hspace{1.5cm} 605 \hspace{1.5cm}$
- Cys Phe Gly Glu Asp Val Cys Ile Ser Ile Pro Glu Val Asp Ala Tyr 610 615 620

Val 625	Met	Val	Leu	Gln	Ala 630	Ile	Glu	Pro	Arg	Ile 635	Thr	Leu	Arg	Gly	Thr 640
Asp	His	Phe	Trp	Arg 645	Pro	Ala	Ala	Gln	Phe 650	Glu	Ser	Ala	Arg	Gly 655	Val
Thr	Leu	Phe	Pro 660	Asp	Ile	Lys	Ile	Val 665	Ser	Thr	Phe	Ala	Lys 670	Thr	Glu
Ala	Pro	Gly 675	Asp	Val	Lys	Thr	Thr 680	Asp	Pro	Lys	Ser	Glu 685	Val	Leu	Glu
Glu	Met 690	Leu	His	Asn	Leu	Asp 695	Phe	Cys	Asp	Ile	Leu 700	Val	Ile	Gly	Gly
Asp 705	Leu	Asp	Pro	Arg	Gln 710	Glu	Cys	Leu	Glu	Leu 715	Asn	His	Ser	Glu	Leu 720
His	Gln	Arg	His	Leu 725	Asp	Ala	Thr	Asn	Ser 730	Thr	Ala	Gly	Tyr	Ser 735	Ile
Tyr	Gly	Val	Gly 740	Ser	Met	Ser	Arg	Tyr 745	Glu	Gln	Val	Leu	His 750	His	Ile
Arg	Tyr	Arg 755	Asn	Trp	Arg	Pro	Ala 760	Ser	Leu	Glu	Ala	Arg 765	Arg	Phe	Arg
Ile	Lys 770	Cys	Ser	Glu	Leu	Asn 775	Gly	Arg	Tyr	Thr	Ser 780	Asn	Glu	Phe	Asn
Leu 785	Glu	Val	Ser	Ile	Leu 790	His	Glu	Asp	Gln	Val 795	Ser	Asp	Lys	Glu	His 800
Val	Asn	His	Leu	Ile 805	Val	Gln	Pro	Pro	Phe 810	Leu	Gln	Ser	Val	His 815	His
Pro	Glu	Ser	Arg 820	Ser	Ser	Ile	Gln	His 825	Ser	Ser	Val	Val	Pro 830	Ser	Ile
Ala	Thr	Val 835	Val	Ile	Ile	Ile	Ser 840	Val	Суѕ	Met	Leu	Val 845	Phe	Val	Val

Ala Met Gly Val Tyr Arg Val Arg Ile Ala His Gln His Phe Ile Gln 855 850 Glu Thr Glu Ala Ala Lys Glu Ser Glu Met Asp Trp Asp Asp Ser Ala 870 Leu Thr Ile Thr Val Asn Pro Met Glu Lys His Glu Gly Pro Gly His 885 890 Gly Glu Asp Glu Thr Glu Gly Glu Glu Glu Glu Ala Glu Glu Glu 900 905 Met Ser Ser Ser Gly Ser Asp Ser Glu Glu Glu Glu Glu Glu Glu 920 Glu Gly Met Gly Arg Gly Arg His Gly Gln Asn Gly Ala Arg Gln Ala 935 Gln Leu Glu Trp Asp Asp Ser Thr Leu Pro Tyr 950 <210> 4 <211> 27 <212> PRT <213> human <400> 4 Ala Ala Gln Pro Gln Phe Val His Pro Glu His Arg Ser Phe Val Asp 1 5 10 Leu Ser Gly His Asn Leu Ala Asn Pro His Pro 20 <210> 5 <211> 28 <212> PRT <213> human <400> 5 Ala Ala Gln Pro Gln Phe Val His Pro Glu His Arg Ser Phe Val Asp 15 5 10

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Leu Ser Gly His Asn Leu Ala Asn Pro His Pro Phe

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Ser Thr Ala Thr
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Leu Ala Asn Pro His Pro
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1 5
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                                10
Glu Val His His Gln Lys Leu Val Phe Phe Ala Glu Asp Val Gly Ser
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20

Phe Val His Pro Glu His Arg Ser Phe Val Asp Leu Ser Gly His Asn

Asn Lys Gly Ala Ile Ile Gly Leu Met Val Gly Gly Val Val Ile Ala  $35 \hspace{1.5cm} 40 \hspace{1.5cm} 45$ 

Thr Val Ile Val Ile Thr Leu Val Met Leu Lys Lys Gln Tyr Thr 50 60

Ser Ile His His Gly Val Val Gln Asn 65 70

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Ser Thr Ala Thr Val

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Ser Thr Ala Thr Val Val 35

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Leu Ser Gly His Asn Leu Ala Asn Pro His Pro Phe Ala Val Pro 20 25 30

Ser Thr Ala Thr Val Val Ile Val 35 40